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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,377	06/19/2006	Catherine J. Pachuk	051058-034000-US	3823

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EXAMINER	
PENG, BO	

ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/560,377	PACHUK ET AL.	
	Examiner	Art Unit	
	BO PENG	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 December 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *63-67,78,79 and 98-101* is/are pending in the application.

4a) Of the above claim(s) *98-101* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *63-67,78 and 79* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This Office action is in response to the amendment filed on December 4, 2009. Claims 1-62, 68-77 and 80-97 have been cancelled. New Claims 98-101 have been added.

2. New Claims 98-101 are directed to a method for inhibiting expression of HBV in a mammalian cell using double-stranded RNA effectors of SEQ ID NOs: 18-22, which are subject matter of previously withdrawn and now cancelled Claims 32-52 (Group I). Claims 98-101 are different from originally elected method for inhibiting expression of HBV in a mammalian cell using double-stranded RNA effectors of SEQ ID NOs: 3 and 10 for the same reason set forth in Para 5 and 6; the Restriction requirement dated June 13, 2008; and Para 3, the Office action dated July, 1 2009. Since Applicant has received an action on the merits for the originally presented invention of Group IV, this invention has been constructively elected by original presentation for prosecution on the merits. Therefore, Claims 98-101 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP 821.03. Accordingly, Claims 63-67, 78 and 79 are considered in this Office action.

Specification

New Matter

3. (**Prior objection-maintained**) The objection to the specification is maintained. Applicant argues that Applicant provides a copy of the PCT specification (from PCT/US04/019229) to serve as a substitute specification. Also Applicant submits a petition, and a new version of the specification concurrently requesting the generation of

a CIP application of parent PCT/US04/019229 that claims the benefit of priority from and incorporates disclosure contained in that PCT and U.S. Provisional 60/638,294.

4. It is noted that Applicant's petition has been dismissed by the decision on July 30, 2010. However, Applicant has not canceled the new version of the specification. Applicant has not cancelled new Fig. 15 and all additional sequences that are not present in PCT/US04/19229 and 60/478,076. The objection is maintained. Applicant is required to cancel all new matters.

5. (**Prior objection-maintained**) The objection to the specification for containing trademarks is maintained because Applicant has failed to correct them.

Claim Rejections - 35 USC 102

6. The following is a quotation of the appropriate paragraphs of 35 USC 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. (**Prior rejection-maintained**) The rejection of Claims 63 and 78 under 35 USC 102(b) as being anticipated by Ill (US 5,843,770), **is maintained** for the reason of record and the reason set forth below:

In response to Applicant's argument:

8. Applicant argues that the examiner has misinterpreted the term "dsRNA" as single-stranded nucleic acid molecules. Applicant argues that, in the PCT specification recites: "By 'dsRNA' is meant a nucleic acid containing a region of two *or more nucleotides that are in a double stranded conformation."* Thus, the Office Action's interpretation that the dsRNA molecule as presently claimed encompasses single stranded

nucleic acid molecules is not correct.

9. This argument is not persuasive because first, Applicant has mischaracterized the Examiner's position by confusing "single stranded nucleic acid molecule" with "conformation". In the previous office action, Para 14, the Examiner states: "In view of the specification, the claimed dsRNA can be in a form of double stranded DNA, DNA/RNA hybrid, single stranded DNA or RNA". One of ordinary skill in the art knows that a single stranded nucleic acid can still form "a double-stranded conformation" when there are proper CG or AU base pars within its own sequence or with a target sequence. The examiner has never indicted that dsRNA is in a single stranded "conformation". Thus, Applicant's argument based on mischaracterizing the Examiner's position is not accurate, therefore not persuasive.

10. Secondly, Applicant is arguing the inherent property of dsRNA. Forming "in a double-stranded conformation" of a RNA is an inherent property of RNA. In other words, an RNA would form "in a double-stranded conformation", when there are proper CG or AU base pars within its own sequence or with a target sequence.

According to MPEP 2112.0, "Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the prima facie case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product".

In the present case, the claims are directed to use of a dsRNA effector molecule comprising at least 19 contiguous base pair nucleotide sequence in a double-stranded conformation from with SEQ ID NO: 3 or SEQ ID NO: 10. As indicated in the previous

Office action, the antisense SEQ ID NO: 1 of the prior art comprises "at least 19 contiguous base pair nucleotide sequence of the claimed dsRNA SEQ ID NO: 10. Forming "a double-stranded conformation" is an inherent property of SEQ ID NO: 1. Since SEQ ID NO: 1 of the prior art is the antisense sequence of SEQ ID NO: 10 of the instant application, it must have the ability to form "a double-stranded conformation" like the instant SEQ ID NO: 1. Thus, Applicant's argument is not persuasive.

11. (**Prior rejection-maintained**) The rejection of Claims 63 and 78 under 35 USC 102(b) as being anticipated by Sallberg (US20020155124, published on October 24, 2002: Now US Pat. 6,680,059), is **maintained** for the reason of record.

In response to Applicant's argument:

12. Applicant presents the same argument as that summarized in Para 10 above. However, this argument has been found not persuasive for the reasons set forth in Para 11 and 12 above. Applicant's same argument to traverse Sallberg's reference is also found not pervasive for the reason discussed in Para 11.

13. Sallberg teaches methods of enhancing the immune response of an animal, including humans, using HBV nucleic acid-based antigen and antiviral drug Ribavirin, wherein said nucleic acid-based antigens include a nucleotide sequence of HBV SEQ ID No: 14, see e.g. [0017] and [0041]. Sallberg also teaches that a nucleic acid-based antigen can comprise at least 9-25, 25-50, 50-100, 100-200, 200-500, 500-1000, 1000-2000, or 2000-4000 consecutive nucleotides of any one of SEQ ID NO: 14 or an RNA that corresponds to these sequences. (Claims 63 and 78), See attached sequence alignment.

Sallberg teaches that HBV nucleic acid-based antigen, including SEQ ID NO: 14 and its fragments, is cloned into an expression vector, see e.g. Para [0040].

14. Sallberg has inherently taught the claimed dsRNA of SEQ ID NO: 3, because he has disclosed the nucleic acid-based antigen SEQ ID NO: 14, which comprises "a double-stranded RNA effector molecule **comprising** an at least 19 contiguous base pair nucleotide sequence... SEQ ID NO: 3, wherein U is substituted for T". As defined by the specification Para [0049], the claimed dsRNA effector molecule can be in the form of a double stranded DNA, DNA/RNA hybrid, or a single stranded RNA. Given that the HBV nucleic acid-based antigen comprising SEQ ID NO: 14 and its fragments of the prior art is in the form of double stranded DNA, and they can form DNA/RNA hybrids, or mRNA (a single stranded RNA) *in vivo*, the HBV nucleic acid-based antigens of the prior art meet the structural limitation of the claimed dsRNA effector molecules. Thus, Sallberg's method of using the HBV nucleic acid-based antigen comprising SEQ ID NO: 14 and its fragments for inhibiting HBV *in vivo* anticipate the instant Claims 63 and 78. The rejection is therefore maintained.

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 USC 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. (**Prior rejection-maintained**) The rejection of Claims 63-67, 78 and 79 under 35 USC 103(a) as being unpatentable over Ill (US 5,843,770), Sallberg (US2002/0155124),

and McCaffrey (Nature Biotechnology, 21(6):639-644; published online May 12, 2003),

is maintained for the reason of record.

In response to Applicant's arguments:

Applicant argues that (1) the Office Action has incorrectly concluded that the term "dsRNA" encompasses single stranded RNA in a single-stranded conformation. (2) the Ill *et al*. and Sallberg *et al*. references do not teach double stranded RNA corresponding to any sequence, let alone double stranded RNA comprising at least 19 contiguous base pair nucleotide sequence in a double-stranded conformation from within a sequence selected from the group consisting of SEQ ID NO: 3 and SEQ ID NO: 10, wherein U is substituted for T; (3) McCaffrey does not teach SEQ ID NOs: 3, 10 and 18-22. (4) The instant application SEQ ID NOs: 18-22 show inhibiting activity against HBV.

17. Regarding Applicant's argument (1), this argument have been found not persuasive for the reason set forth in Para 9 and 10 above.

18. Regarding Applicant's argument (2), this argument is not persuasive for the reason set forth in Para 10 and 13 above.

19. Applicant's argument (3) against McCaffrey is not persuasive, either. First, the cited Ill and Sallberg references teach dsRNA effector molecules comprising at least 19 contiguous base pair nucleotide sequence in a double-stranded conformation from with SEQ ID NO: 3 or SEQ ID NO: 10. Secondly, SEQ ID NOs: 18-22 are non-elected inventions, and have not been examined.

20. Regarding Applicant's argument (4), it is expected that two "dsRNA effector molecule comprising at least 19 contiguous base pair nucleotide sequence in a double-stranded conformation with SEQ ID NO: 3 and SEQ ID NO: 10" would have the ability to inhibit HBV in view of Ill, Sallberg and McCaffrey. Specifically, Ill teaches that an expression plasmid encoding one or more antisense transcripts (dsRNA effector molecule), which comprises the claimed SEQ ID NO: 10, can inhibit HBV production in

mice. Sallberg teaches HBV nucleic acid-based antigen SEQ ID NO: 14, and its fragments, which comprises the claimed dsRNA effector molecule comprising SEQ ID NO: 3, can be used for inhibiting HBV *in vivo*. McCaffrey shows that each shRNA (dsRNA) targets the HBV pregenomic RNA, the mRNA for the core antigen and the polymerase, as well as the X region and its transcript, can inhibit HBV in cell cultures. McCaffrey also demonstrated that dsRNA is capable of inhibiting HBV replication in mice. Based on the prior art teachings, those of ordinary skill in the art would have had a reasonable expectation of success in using two dsRNA comprising SEQ ID NOs: 3 and 10 for inhibiting HBV *in vivo*. In turn, because the claimed oligonucleotides have the properties predicted by the prior art, it would have been obvious for one of skill in the art to make such dsRNA effector molecules for inhibiting HBV *in vivo*. The rejection is maintained.

Remarks

21. No claim is allowed. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bo Peng, Ph.D. whose telephone number is 571-272-5542. The examiner can normally be reached on Tu-F, 8:30-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Zachariah Lucas can be reached on 571-272-0905. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/BO PENG/
Primary Examiner, Art Unit 1648